

REMARKS / ARGUMENTS

Claims 1-6 and 10- 20 are pending. No amendments are entered by way of this response. A Listing of Claims is provided herewith for the convenience of the Examiner in consideration of this response.

35 USC §103

That Examiner has maintained the rejection of claims 1-6 and 10-20 under 35 USC § 103 as allegedly unpatentable over US Patent Application Publication No. 2002/0013335 ("Azrolan") in view of UK Patent Application No. GB 2327611 ("Haebelin") and, Decker, 1996 ("Madhavi").

It is substantially asserted that these documents provide the components contained in Applicants' claimed compositions, and that selection of ranges of components for a composition is within the skill in the art.

Applicants respectfully request that the rejection under 35 USC § 103 be withdrawn. MPEP §2143 (Rev. 6, Sept. 2007) defines a number of 'exemplary rationales' that may support a conclusion of obviousness under KSR Int'l Co. v. Teleflex Inc. (550 U.S. ____ (2007), 127 S. Ct. 1727), including:

- (A) Combining prior art elements according to known methods to yield predictable results; . . .
- (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; . . . and
- (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art teachings to arrive at the claimed invention; . . .

Applicants respectfully assert that none of these exemplary rationales is met by the combination of documents relied upon by the Examiner.

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A brief summary of the documents relied upon by the Examiner is as follows. The combination of these documents is analyzed under the 'exemplary rationales' identified above in the sections that follow.

Azrolan describes methods of treating cardiovascular disease with a rapamycin which may include CCI-779. General information regarding excipients useful in formulations is provided. Haeberlin provides for stabilization of macrolides, including rapamycins generally, by formulation with an acid such as malonic acid. Madhavi describes the use of BHA and BHT in the food industry (page 277, second paragraph).

A. Combining prior art elements according to known methods to yield predictable results

As stated in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ____ (2007), 127 S. Ct. 1727 at 1741:

“...a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art....it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.”

Haeberlin and Madhavi do not add anything to Azrolan which would predictably yield the solid CCI-779 compositions presently claimed. None of these documents even recognizes the problem to which the present invention is directed, *i.e.*, providing a highly bioavailable non-micronized CCI-779 formulation that avoids both dissolution and instability problems associated with the formation of the CCI-779 compositions of the prior art by compression. In the absence of any recognition of the underlying problem or of the beneficial results of the claimed compositions that address these problems, one of skill in the art could not have combined the 'prior art elements' to yield 'predictable results'.

E. "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success

Applicants note that the Examiner has not expressly presented this line of reasoning. However, given that the Examiner relies on three documents as describing all the components of the claimed compositions, Applicants point out that the documents relied upon by the Examiner provide an extensive number of *possible* solutions (not including the specific ranges of components identified in the claims), with no particular combination lending a reasonable expectation of success (absent impermissible hindsight).

G. Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art teachings to arrive at the claimed invention

The Examiner has not provided any motivation to combine these documents to arrive at the claims presently pending. Absent the Applicants' recognition of the problem on which this invention focuses, nothing in the cited documents suggests the combination of excipients provided by the present formulation, nor could the advantages thereof be predicted. Further, it is not routine within the art to select components, which may or may not have been identified previously, and then derive a formulation of those components in order to solve a problem unrecognized in the art.

The Examiner's assertion that one would combine Azrolan with Madhavi because "BHA and BHT are extensively used antioxidants," fails to supply any actual reason to combine. Similarly, that Haeberlin describes the use of acids to stabilize macrolides does not itself supply any motivation to combine with Azrolan. See KSR Int'l Co. v. Teleflex, *supra*. The Examiner has provided no reason to combine these documents, except via hindsight to reject Applicants' claimed compositions.

Even if combined, the determination of what percentage of each component to include in the composition could not be derived from these documents

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by one of skill in the art. Contrary to the Examiner's position at page 8, last paragraph, it is the inventive selection of components and amounts of same in order to solve the problems identified by the Applicants that yielded the presently claimed compositions.

The Examiner's arguments thus fail to support any rationale under *KSR v. Teleflex* supporting the present obviousness rejection that couldn't be equally (and improperly) applied to any new composition of elements. Accordingly, for the reasons set forth above, the Examiner is respectfully requested to reconsider and withdraw the rejection under 35 USC 103(a).

Double Patenting

Claims 1, 2-6, and 20 are provisionally rejected on the ground of non-statutory obviousness-type double patenting over claims 55, 58-61, 65 and 72-73 of copending Application No. 10/930,487 in view of Azrolan.

Applicants respectfully traverse this rejection.

Copending application 10/930,487 contains claims drawn to formulations containing amorphous CCI-779. Azrolan describes methods of treating cardiovascular disease with a rapamycin which may include CCI-779, and includes general information regarding excipients useful in formulations is provided. There is no motivation to combine Azrolan with copending application 10/930,487.

In contrast, the present application contains claims to CCI-779 with the specified excipients. Applicants believe that the claims of the two applications, in view of Azrolan, are nonobvious over the other. The Examiner's assertion that combination would be obvious to one of skill in the art provides only a legal conclusion, absent any reason for combining that could be found outside of Applicants' disclosure.

Reconsideration and withdrawal of this rejection is requested.

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Claims 1, 2-6, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-8 and 11 of copending application no. 11/030,685 in view of Azrolan.

Copending application 11/030,658 contains claims drawn to micronized CCI-779 and formulations containing same. Azrolan describes methods of treating cardiovascular disease with a rapamycin which may include CCI-779, and includes general information regarding excipients useful in formulations is provided. There is no motivation to combine Azrolan with copending application 11/030,658.

In contrast, the present application contains claims to non-micronized CCI-779 with the specified excipients. Applicants believe that the claims of the two applications, in view of Azrolan, are nonobvious over each other. The Examiner's assertion that combination would be obvious to one of skill in the art provides only a legal conclusion, absent any reason for combining that could be found outside of Applicants' disclosure.

Reconsideration and withdrawal of this rejection is requested.

Claims 1, 2, 4, and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-16 and 19 of copending application no. 10/626,943.

Copending application no. 10/626,943 contains claims drawn to parenteral formulations comprising CCI-779, an alcoholic solvent, an antioxidant, a diluent solvent, and a surfactant. In contrast, the present application contains claims to compositions of CCI-779 with the specified excipients. Applicants believe that the claims of the two applications are nonobvious over each other.

The Examiner's assertion that combination would be obvious to one of skill in the art provides only a legal conclusion, absent any reason for combining that could be found outside of Applicants' disclosure.

Reconsideration and withdrawal of this rejection is requested.

In view of these remarks, Applicants respectfully request favorable consideration of the claims.

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The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

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